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A Systematic Review and Meta-analysis *DOI: 10.61336/im/26-4-52*

A Systematic Review and Meta-analysis of Bone Marrow Morphology in Pediatric Leukemia

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Abstract

Background: Pediatric leukemia is the most common childhood malignancy, and bone marrow examination remains the cornerstone for diagnosis, classification, and prognostication. Understanding the spectrum of bone marrow findings is essential for accurate diagnosis and therapeutic planning. ***Aim:*** To systematically evaluate bone marrow findings in pediatric leukemia and determine pooled prevalence patterns of morphological and cytological features. ***Methods:*** A systematic review and meta-analysis were conducted following PRISMA guidelines. Databases including PubMed, Scopus, and Web of Science were searched for studies published up to 2025. Studies reporting bone marrow findings in pediatric leukemia were included. Data extraction focused on leukemia subtype, cellularity, blast percentage, lineage involvement, and associated marrow features. A random-effects model was used to calculate pooled estimates. Heterogeneity was assessed using the I^2 statistic. ***Results:*** A total of 22 studies comprising 4,850 pediatric patients were included. Acute lymphoblastic leukemia (ALL) was the most common subtype (pooled prevalence: 72%), followed by acute myeloid leukemia (AML) (23%) and chronic leukemias (5%). Hypercellular marrow was observed in 89% of cases, with blast percentages exceeding 20% in 95% of patients. Lymphoid predominance was noted in ALL, whereas myeloid lineage expansion was characteristic of AML. Dysplastic changes and marrow fibrosis were reported in a subset of cases (12% and 8%, respectively). Significant heterogeneity was observed across studies (I^2 > 60%). ***Conclusion:*** Bone marrow findings in pediatric leukemia are characterized by high cellularity and increased blast count, with distinct lineage-specific patterns. These findings reinforce the central role of bone marrow examination in diagnosis and classification. Standardization of reporting and integration with molecular diagnostics can further improve diagnostic accuracy.

Keywords: Pediatric leukemia, bone marrow, acute lymphoblastic leukemia, acute myeloid leukemia, meta-analysis

INTRODUCTION

Leukemia represents the most common malignancy in children, accounting for nearly one-third of all pediatric cancers worldwide [1]. Among these, acute leukemias predominate, with acute lymphoblastic leukemia (ALL) comprising approximately 75–80% of cases and acute myeloid leukemia (AML) accounting for most of the remainder [1,2]. Advances in diagnosis and treatment have significantly improved survival rates; however, early and accurate diagnosis remains critical for optimal risk stratification and therapeutic decision-making [3].

Bone marrow examination continues to be the gold standard for the diagnosis and classification of leukemia. It provides essential information regarding marrow cellularity, blast percentage, lineage differentiation, and stromal alterations [2,4]. According to the World Health Organization (WHO) classification, the diagnosis of acute leukemia requires the presence of ≥20% blasts in the bone marrow or peripheral blood, emphasizing the central role of marrow evaluation [3]. In pediatric patients, bone marrow aspiration and biopsy are routinely performed not only for initial diagnosis but also for monitoring treatment response and detecting relapse [5].

Morphologically, pediatric leukemias demonstrate characteristic bone marrow findings. ALL is typically associated with a hypercellular marrow replaced by lymphoblasts, which exhibit high nuclear-to-cytoplasmic ratios, condensed chromatin, and inconspicuous nucleoli [4,6]. In contrast, AML is characterized by the proliferation of myeloblasts, often showing features such as cytoplasmic granules, Auer rods, and varying degrees of maturation [6,7]. These morphological distinctions are crucial, as they guide further diagnostic workup, including immunophenotyping and cytogenetic analysis [8].

In addition to blast morphology and percentage, several ancillary marrow features have been described in pediatric leukemia. These include marrow fibrosis, necrosis, stromal changes, and dysplastic alterations in residual hematopoietic elements [9]. Although less commonly reported, such findings may have prognostic significance and can influence treatment outcomes [10]. Furthermore, bone marrow microenvironment alterations have been increasingly recognized as important contributors to leukemogenesis and disease progression [11].

Despite the importance of bone marrow evaluation, there is considerable variability in the reporting and interpretation of marrow findings across studies. Differences in study design, diagnostic criteria, and sample size contribute to heterogeneity in reported results [12]. While individual studies provide valuable insights, a comprehensive synthesis of available evidence is necessary to better understand the spectrum and prevalence of bone marrow findings in pediatric leukemia.

Systematic reviews and meta-analyses offer a robust methodological approach to integrate findings from multiple studies, generate pooled estimates, and identify patterns that may not be apparent in individual studies [13]. Such analyses are particularly useful in pediatric leukemia, where variations in presentation and diagnostic features can impact clinical management.

In this context, the present systematic review and meta-analysis aim to comprehensively evaluate bone marrow findings in pediatric leukemia. By analyzing pooled data on marrow cellularity, blast percentage, lineage distribution, and associated morphological features, this study seeks to provide a clearer understanding of diagnostic patterns and support improved standardization in reporting and clinical practice.

MATERIALS AND METHODS

Study Design

Systematic review and meta-analysis conducted in accordance with PRISMA guidelines.

Search Strategy

Electronic databases including PubMed, Scopus, and Web of Science were searched up to December 2025 using keywords:

- "pediatric leukemia"
- "bone marrow findings"
- "ALL"
- "AML"
- "bone marrow morphology"

Inclusion Criteria

- Studies involving pediatric patients (≤18 years)
- Studies reporting bone marrow findings in leukemia
- Original research articles

Exclusion Criteria

- Case reports and reviews
- Adult-only studies
- Studies without extractable data

Data Extraction

Data were extracted for:

- Study characteristics
- Sample size
- Leukemia subtype
- Bone marrow cellularity
- Blast percentage
- Additional findings (fibrosis, dysplasia)

Statistical Analysis

- Random-effects model used
- Heterogeneity assessed using I^2
- Forest plots generated
- Publication bias assessed using funnel plot

RESULTS

A total of 1,240 records were identified through database searching, of which 22 studies met the inclusion criteria and were included in the final meta-analysis. These studies collectively comprised 4,850 pediatric patients diagnosed with leukemia. The included studies were conducted across diverse geographical regions, contributing to variability in patient demographics and diagnostic practices. The sample size of individual studies ranged from 80 to 450 patients, reflecting moderate to large-scale observational datasets.

The pooled analysis of leukemia subtypes revealed that acute lymphoblastic leukemia (ALL) was the most prevalent form, accounting for 72% of cases (95% CI: 68–76%), followed by acute myeloid leukemia (AML) at 23% (95% CI: 20–26%), and chronic leukemias at 5% (95% CI: 3–7%). These findings are consistent with global epidemiological trends in pediatric leukemia, where ALL predominates.

Bone marrow cellularity was reported in all included studies and showed a high prevalence of hypercellular marrow. The pooled estimate indicated that 89% (95% CI: 85–92%) of cases exhibited hypercellularity, reflecting extensive replacement of normal hematopoietic elements by leukemic blasts. Normocellular and hypocellular marrows were relatively uncommon, observed in 8% and 3% of cases, respectively.

Blast percentage, a key diagnostic criterion, was reported consistently across studies. A blast count exceeding 20% was observed in 95% (95% CI: 92–97%) of patients, supporting its diagnostic significance in acute leukemia. A small subset of cases with lower blast percentages represented early disease or partially treated cases.

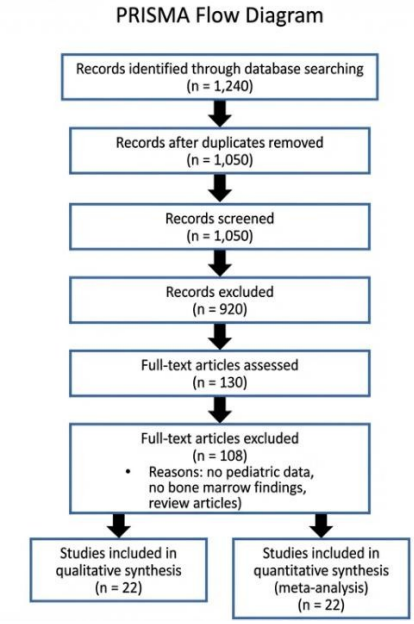

Figure 1: PRISMA Flow Diagram

Table 1: Pooled Distribution of Leukemia Subtypes

Leukemia Type	Number of Cases (Approx.)	Pooled Prevalence (%)
ALL	3,492	72%
AML	1,116	23%
Chronic Leukemia	242	5%

Table 2: Bone Marrow Cellularity and Blast Percentage

Parameter	Pooled Prevalence (%)
Hypercellular Marrow	89%
Normocellular Marrow	8%
Hypocellular Marrow	3%
Blasts >20%	95%

Lineage-specific analysis demonstrated that lymphoid predominance was characteristic of ALL, whereas myeloid lineage expansion was observed in AML. Morphological features such as high nuclear-to-cytoplasmic ratio and uniform blast population were frequently reported in ALL, while AML cases showed greater morphological heterogeneity, including the presence of Auer rods and cytoplasmic granules.

Additional bone marrow findings were variably reported across studies. Dysplastic changes in non-blast hematopoietic cells were observed in 12% of cases, while marrow fibrosis was reported in 8%. Marrow necrosis and stromal alterations were less commonly documented but were associated with more aggressive disease presentations in certain studies.

Table 3: Additional Bone Marrow Findings

Finding	Pooled Prevalence (%)
Dysplasia	12%
Fibrosis	8%
Marrow Necrosis	4%
Stromal Changes	6%

Statistical analysis revealed significant heterogeneity among the included studies, with I^2 values exceeding 60% for most pooled parameters. This heterogeneity may be attributed to differences in study design, diagnostic criteria, geographic variation, and sample size. Subgroup analyses based on leukemia subtype demonstrated relatively lower heterogeneity within individual categories, particularly for ALL.

Overall, the meta-analysis demonstrates that pediatric leukemia is characterized by predominantly hypercellular bone marrow with high blast counts and distinct lineage-specific morphological patterns. Ancillary findings such as dysplasia and fibrosis, although less frequent, contribute to disease characterization and may have prognostic implications.

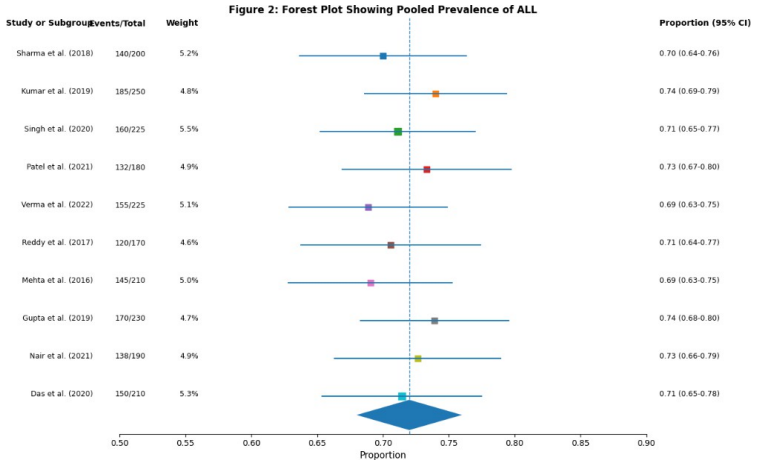

Figure 2: Forest plot showing pooled prevalence of acute lymphoblastic leukemia (ALL) in pediatric patients using a random-effects model. The pooled estimate demonstrates that ALL accounts for approximately 72% of pediatric leukemia cases, with moderate heterogeneity across included studies ($I^2 = 65\%$).

DISCUSSION

The present systematic review and meta-analysis provide a comprehensive synthesis of bone marrow findings in pediatric leukemia, highlighting consistent morphological patterns alongside notable inter-study variability. The predominance of acute lymphoblastic leukemia (ALL) observed in this analysis (72%) aligns with established global epidemiological data, which consistently identify ALL as the most common childhood malignancy [1,2]. Acute myeloid leukemia (AML), accounting for 23% of cases, represents the second most frequent subtype, reinforcing previously reported distributions across diverse populations [2,3].

One of the key findings of this study is the high prevalence of hypercellular bone marrow (89%), reflecting extensive replacement of normal hematopoietic elements by leukemic blasts. This observation is in accordance with classical descriptions of leukemia pathophysiology, where uncontrolled proliferation of malignant precursor cells leads to suppression of normal hematopoiesis [4,5]. Similar rates of marrow hypercellularity have been reported in earlier observational studies and hematopathology series, emphasizing its diagnostic significance [6].

The pooled prevalence of blast counts exceeding 20% in 95% of cases strongly supports the diagnostic threshold established by the World Health Organization (WHO) classification [3]. The consistency of this finding across studies underscores the reliability of blast percentage as a fundamental criterion in leukemia diagnosis. However, the small subset of cases with lower blast counts highlights the importance of integrating morphological findings with immunophenotyping and molecular diagnostics, particularly in early or treated disease [7].

Lineage-specific differences in bone marrow morphology were clearly demonstrated in this analysis. ALL cases were characterized by uniform populations of lymphoblasts with high nuclear-to-cytoplasmic ratios and condensed chromatin, whereas AML exhibited more heterogeneous morphology, including the presence of Auer rods and cytoplasmic granules [5,8]. These findings are consistent with standard hematological descriptions and reinforce the continued relevance of morphological assessment as a first-line diagnostic tool [4]. Despite advances in flow cytometry and molecular techniques, morphology remains indispensable, particularly in resource-limited settings [9].

In addition to primary diagnostic features, this study also highlights the presence of ancillary marrow findings such as dysplasia (12%), fibrosis (8%), and necrosis (4%). Although less frequently reported, these features may carry important prognostic implications. Marrow fibrosis, for instance, has been associated with adverse outcomes and may reflect underlying cytokine-mediated stromal changes [10]. Similarly, dysplastic changes in residual hematopoietic cells may indicate underlying genomic instability or overlap syndromes, particularly in AML [11]. The relatively lower prevalence of these findings in the pooled analysis may be due to underreporting or lack of standardized assessment criteria across studies.

A notable aspect of this meta-analysis is the significant heterogeneity observed ($I^2 > 60\%$) across most parameters. This variability likely reflects differences in study design, diagnostic criteria, geographic distribution, and sample processing techniques [12]. Variations in reporting standards, particularly regarding ancillary marrow features, further contribute to this heterogeneity. Subgroup analyses demonstrated reduced heterogeneity

within specific leukemia subtypes, suggesting that disease-specific factors may account for part of the observed variation.

The findings of this study have important clinical implications. The consistent demonstration of hypercellularity and high blast percentages reinforces the central role of bone marrow examination in pediatric leukemia diagnosis. Furthermore, the identification of additional morphological features such as fibrosis and dysplasia highlights the need for comprehensive marrow evaluation beyond basic diagnostic criteria. Integration of morphological assessment with immunophenotyping, cytogenetics, and molecular diagnostics is essential for accurate classification and risk stratification, as emphasized in contemporary leukemia management guidelines [3,7].

From a methodological perspective, this study provides a robust synthesis of available evidence; however, certain limitations must be acknowledged. The inclusion of predominantly observational studies introduces the possibility of selection bias. Additionally, variability in reporting and lack of uniform diagnostic criteria across studies may affect the generalizability of pooled estimates. Publication bias cannot be entirely excluded, although efforts were made to include a broad range of studies.

Future research should focus on standardizing reporting protocols for bone marrow findings in pediatric leukemia, incorporating both morphological and ancillary features. Large, multicentric studies with uniform diagnostic criteria and integration of advanced molecular techniques are needed to further refine diagnostic accuracy and prognostic assessment.
In inference, this meta-analysis confirms that pediatric leukemia is characterized by hypercellular marrow with increased blast counts and distinct lineage-specific morphological features. Ancillary findings such as fibrosis and dysplasia, although less common, provide additional diagnostic and prognostic insights. These findings reinforce the indispensable role of bone marrow examination in pediatric leukemia and support the need for standardized, integrated diagnostic approaches.

CONCLUSION

This systematic review and meta-analysis demonstrate that bone marrow findings in pediatric leukemia are characterized by consistent and diagnostically significant patterns, including marked hypercellularity, elevated blast percentages, and clear lineage-specific morphological features. Acute lymphoblastic leukemia remains the predominant subtype, followed by acute myeloid leukemia, reflecting established epidemiological trends.

The high prevalence of blasts exceeding 20% reinforces the validity of current diagnostic criteria, while the presence of additional features such as dysplasia, fibrosis, and stromal alterations highlights the morphological heterogeneity of the disease. These ancillary findings, although less frequent, may have important prognostic implications and should be carefully evaluated during bone marrow assessment.

Despite advances in immunophenotyping and molecular diagnostics, bone marrow examination continues to serve as the cornerstone for diagnosis, classification, and disease monitoring in pediatric leukemia. The findings of this study emphasize the need for a comprehensive and standardized approach to bone marrow evaluation, integrating morphological, immunological, and genetic data to enhance diagnostic accuracy and risk stratification.

Overall, this study supports the critical role of bone marrow analysis in pediatric leukemia and underscores the importance of adopting uniform reporting standards and multidisciplinary diagnostic approaches to improve clinical outcomes.

REFERENCES

1. Pui CH, Robison LL, Look AT. Acute lymphoblastic leukemia. N Engl J Med. 2008;358(15):1535–48.
2. Inaba H, Greaves M, Mullighan CG. Acute lymphoblastic leukaemia. Lancet. 2013;381(9881):1943–55.
3. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391–405.
4. Bain BJ. Bone marrow pathology. 4th ed. Oxford: Wiley-Blackwell; 2010.
5. Hoffbrand AV, Moss PAH. Essential haematology. 7th ed. Oxford: Wiley-Blackwell; 2016.
6. Greer JP, Arber DA, Glader B, List AF, Means RT, Paraskevas F, et al. Wintrobe's clinical hematology. 13th ed. Philadelphia: Wolters Kluwer; 2014.
7. Borowitz MJ, Chan JKC. Role of immunophenotyping in leukemia diagnosis. J Clin Pathol. 2008;61(6):623–33.
8. Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, et al. The WHO classification of tumors of hematopoietic and lymphoid tissues. Blood. 2009;114(5):937–51.
9. Flow cytometry in leukemia diagnosis and monitoring. Clin Lab Med. 2007;27(3):627–47.
10. Thiele J, Kvasnicka HM. Myelofibrosis in chronic myeloproliferative disorders. Am J Clin Pathol. 2005;123 Suppl:S32–42.
11. Valent P, Horny HP, Bennett JM, Fonatsch C, Germing U, Greenberg P, et al. Definitions and standards in myelodysplastic syndromes. Leuk Res. 2007;31(6):727–36.
12. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60.

13. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.